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May 28, 1993

By Ann Lovell

#19  
SNC  
6/03/93  
**PATENT**

Attorney Docket No. 15422-70

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: )

Higuchi, et al. )

Serial No.: 07/695,201 )

Filed: May 2, 1991 )

For: HOMOGENEOUS METHODS FOR )  
NUCLEIC ACID AMPLIFICATION )  
AND DETECTION )

Examiner: R. Prouty

Art Unit: 1814

DECLARATION PURSUANT TO 37  
C.F.R. § 1.132

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

I, Louis M Mezei, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. § 1001, and may jeopardize the validity of the subject patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true and statements made on information or belief are believed to be true.

2. I am a co-inventor with John W. H. Sutherland and Patrick Sheridan of U.S. Patent No. 5,049,490 ['490].

3. I understand that the '490 patent is cited as prior art against the subject patent. I have not reviewed the subject patent application. I have been asked to comment on language of Example 6 of the '490 patent. I have personally reviewed this example and understand that the Examiner finds the example to describe the addition of intercalating agents into the polymerase chain reaction [PCR].

5/21/93

~~In particular, the Examiner relies on the following language:~~

In particular, the Examiner relies on the following language:  
The polymerase chain reaction was then initiated by the addition of aliquotes of DNA polymerase, and fluorescent signals were measured continuously over time.

This passage recites an error which is obvious to scientists familiar with PCR. It is an inadvertent misuse of scientific language. We were not carrying out PCR in this example. We were merely using PCR reagents. PCR is an amplification procedure which requires an excess amount of two primers and repeated thermal cycling to permit annealing and denaturing of primers and extension product.

In contrast, the Sutherland *et al.* patent is directed to measuring the amount of polymerase present in a sample. In the process of developing commercial kits, Cetus\Kodak (the assignees of the Sutherland patent) were interested in better ways of measuring the amount of polymerase present in our PCR products. The reagents used in Example 6 are PCR reagents not because the investigators intended to measure amplification target during PCR but because they wanted measure the amount of polymerase in PCR mixtures.

The passage relied upon by the Examiner and cited above is clearly an error in language. PCR was not described in that passage or anywhere else in the application. It is beyond question that the recited reaction mixture of example 6 has only one primer and the assay described does not involve thermal cycling.

This Declarant has nothing further to say.

Dated: 5/21/95

Louis M Mezei  
Louis M Mezei